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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,105	10/30/2003	Jerome B. Zeldis	9516-073-999	1860

20583 7590 09/05/2008

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EXAMINER
CHONG, YONG SOO

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
09/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/699,105	ZELDIS, JEROME B.	
	Examiner	Art Unit	
	YONG S. CHONG	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 2 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,5,9,22,23 and 26-34* is/are pending in the application.

4a) Of the above claim(s) *3,4,6-8,10-21,24,25 and 35-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,5,9,22,23 and 26-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/10/08 has been entered.

Claim 1 has been cancelled. Claims 2-37 are pending. Claims 3-4, 6-8, 10-21, 24-25, 35-37 have been withdrawn. Claims 2, 5, 9, 22-23, 26-34 are examined herein.

Applicant's arguments have been fully considered but found not persuasive. The rejections of the last Office Action are maintained for reasons of record and repeated below for Applicant's convenience.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim(s) 2, 5, 9 are rejected under 35 U.S.C. 103(a) as being obvious over Bhagwat et al. (WO 02/10137 A2, of record) in view of Hale et al. (US Patent 6,949,580 B2).

The instant claims are directed to a method of treating MD in a patient by administering a compound of formula I.

Bhagwat et al. teach that indazole derivatives of formula I inhibit JNK, a protein kinase (abstract). A preferred compound is 1-(5-(1H-1,2,4-triazol-5-yl)(1H-indazol-3-yl))-3-(2-piperidylethoxy)benzene (example 243, pg. 219).

However, Bhagwat et al. fail to disclose the nexus between protein kinase inhibitors and macular degeneration.

Hale et al. teach that protein kinase inhibitors (col. 1, lines 16-21) are useful for treating ocular diseases such as macular degeneration (col. 21, lines 41-43).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have treated a patient suffering from macular degeneration by administering 1-(5-(1H-1,2,4-triazol-5-yl)(1H-indazol-3-yl))-3-(2-piperidylethoxy)benzene.

A person of ordinary skill in the art would have been motivated to have treated a patient suffering from macular degeneration by administering 1-(5-(1H-1,2,4-triazol-5-yl)(1H-indazol-3-yl))-3-(2-piperidylethoxy)benzene because: (1) Bhagwat et al. discloses 1-(5-(1H-1,2,4-triazol-5-yl)(1H-indazol-3-yl))-3-(2-piperidylethoxy)benzene to be a protein kinase inhibitor and (2) Hale et al. discloses protein kinase inhibitors to be useful for treating macular degeneration. Therefore, a person of ordinary skill in the art would have had a reasonable expectation of success in treating macular degeneration in a patient by administering 1-(5-(1H-1,2,4-triazol-5-yl)(1H-indazol-3-yl))-3-(2-piperidylethoxy)benzene.

Claim(s) 22-23, 26-34 are rejected under 35 U.S.C. 103(a) as being obvious over Bhagwat et al. (WO 02/10137 A2, of record) and Hale et al. (US Patent 6,949,580 B2) as applied to claims 2, 5, 9 in view of Ron et al. (US Patent 6,204,270 B1) and Applicant's admission of the prior art.

The instant claims are directed to a method of treating MD in a patient by administering a compound of formula I along in conjunction with other forms of therapy as stated in claims 22-23.

Bhagwat and Hale et al. teach as discussed above, however, fail to disclose other forms of therapy as stated in claims 22-23.

Ron et al. discloses treatment of macular degeneration, a TNF-alpha related eye disorder (col. 4, lines 21-26), with TNF-alpha inhibitors, such as pentoxifylline (col. 2, lines 59-60) and thalidomide (col. 3, lines 5-6).

Applicant's admission of the prior art discloses two forms of macular degeneration, wet and dry MD (pg. 1, lines 20-31). Also disclosed are known treatments for MD, which include verteporfin, interferon α, rhuFab (pg. 3-4), laser photocoagulation therapy, and photodynamic therapy (pg. 5, lines 27-28).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have combined the treatment regimens as disclosed by Bhagwat, Hale, Ron, and in Applicant's admission of the prior art for a person suffering from macular degeneration.

A person of ordinary skill in the art would have combined the treatment regimens as disclosed by Bhagwat, Hale, Ron, and in Applicant's admission of the prior art for a person suffering from macular degeneration because: (1) all of the treatment regimens are directed to macular degeneration and (2) for the therapeutically additive effect of each individual active agent. Therefore, a person of ordinary skill in the art would have had a reasonable expectation of success in treating macular degeneration in a patient by combining the treatment regimens as disclosed by Bhagwat, Hale, Ron, and in Applicant's admission of the prior art.

"It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... The idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Response to Arguments

Applicant argues that Hale teaches that KDR family kinases are useful for treating ocular diseases. In addition, Hale provides a specific definition for JNK-mediated conditions, which does not include ocular diseases. Hale notes distinct differences in how pathways are activated, specifically pointing to the difference between the activation of the JNK and ERK pathways, therefore providing no reason why one of ordinary skill in the art would use a JNK inhibitor for the treatment of macular degeneration and have a reasonable expectation of success. Applicant argues that the Bhagwat reference teaches that the compounds disclosed therein are selective JNK inhibitors.

This is not persuasive because there is substantial overlap between the diseases associated with JNK and ERK, for example all types of cancer, vascular diseases, and autoimmune diseases. Hale repeatedly teaches that the same compounds of the invention can treat both JNK and KDR mediated diseases. The compounds disclosed by Hale, which are protein kinase inhibitors, are taught to be useful in the treatment of all diseases-mediated by various protein kinases, such as JNK, ERK, and KDR. Examiner notes that these same compounds are useful in every JNK, ERK, or KDR-mediated disease (col. 21, lines 1-2, 30-31). Further support is given by Hale, which states that any protein kinase inhibitor is useful to treat any protein kinase-mediated condition (col. 19, lines 30-35). In this manner, a known protein kinase inhibitor will be useful to treat any disease mediated by protein kinase, no matter whether it is JNK or KDR. Further corroboration for a case of obviousness is provided in the claims of

Bhagwat, where JNK-mediated diseases were disclosed to include rheumatoid arthritis, psoriasis, dermatitis, atherosclerosis, cancers of the brain, stomach, lung, and pancreas. It is these diseases that were also taught to be KDR-mediated conditions by Hale.

Applicant is also reminded that the standard for obviousness is not absolute, but a reasonable expectation of success. Hale clearly states that the present invention relates to protein kinase inhibitors, in general, for the treatment of disease states related to protein kinase inhibitors (col. 1, lines 16-21). Macular degeneration is disclosed to be a disease mediated by KDR, which along with JNK are both protein kinases. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating macular degeneration with a JNK inhibitor.

Examiner notes that this is a typical genus/species situation. Once a *prima facie* case of obviousness is established, the burden is shifted to the Applicant for objective evidence for nonobviousness. See MPEP 2144.08.

Applicant argues against the species/genus situation by citing *In re Baird* case law. Firstly, Applicant is reminded that since Hale teaches protein kinase inhibitors, in general, for the treatment of disease states related to protein kinase inhibitors, it is obvious to treat macular degeneration since it is a disease mediated by KDR, which is a protein kinase. Therefore, since KDR is a species of the genus, protein kinases, it is obvious to treat macular degeneration with 1-(5-(1H-1,2,4-triazol-5-yl)(1H-indazol-3-yl))-3-(2-piperidylethoxy)benzene. Secondly, Examiner asserts that there are a limited

number of species in the genus of protein kinases so that one of ordinary skill in the art can envision each species as it pertains in the method of the instant invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Yong S Chong/
Examiner, Art Unit 1617

YSC